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13. ABSTRACT *(Maximum 200* The purpose of this study is to determine whether the risk of breast cancer is increased among women with tumors that are positive for the tumor marker HER-2/neu and who also have a history of oral contraceptive use, or other risk factors for breast cancer. As recommended by the scientific review committee, other funding has been obtained to expand the number of tumor markers examined; these include p53 and cyclin D1. Study methods include: (i) retrieval of the pathology specimens for 511 cases from over 30 hospitals in the study area; (ii) performing laboratory assays for the tumor markers by immunohistochemistry; and (iii) combining lab results with the previously collected questionnaire data to statistically evaluate the interactions between tumor markers and breast cancer risk factors. Pathology materials have been successfully obtained from over 70% of the hospitals; this includes over one-half of the study cases. Laboratory assays are complete in over a third of all cases. Study progress is on target for completion of the study at the end of year two as planned.

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FOREWORD

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Principal Investigator's Signature

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Date

ANNUAL REPORT FOR YEAR 1: ORAL CONTRACEPTIVE USE AND HER-2/NEU POSITIVE BREAST CANCER AMONG YOUNG WHITE AND BLACK WOMEN (AIBS 2445)

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INTRODUCTION

Study Hypothesis

Do breast cancer cases with tumors that are positive for HER-2/*neu* have a higher risk of breast cancer in relation to oral contraceptives and other risk factors for breast cancer as compared with breast cancer cases without these tumor markers, or women without breast cancer?

Study Plan

Original Design. The study original design has three basic components: (1) to collect paraffin-embedded blocks from participating hospitals for 511 breast cancer cases (that had previously participated in a case-control study in New Jersey conducted by the PI); (2) to perform laboratory assays on the tumor tissue for the tumor marker HER-2/*neu* using immunohistochemical techniques; (3) to combine the lab results with the questionnaire data (that was obtained in the previously conducted case-control study) to complete the statistical analyses.

Modifications. The comments from the scientific reviewers of our U.S. ARMY study proposal were for the most point very enthusiastic about our study plan. One major suggestion was that other tumor markers in addition to HER-2 *neu* should also be included in our laboratory analyses. Since funding from the ARMY for this study began, we have applied and received funding from another source to add laboratory analyses using immunohistochemical techniques for p53 and cyclin D1. Thus, our study hypothesis has been expanded to determine whether breast cancer cases that are positive for HER-2/neu, or p53, or cyclin D1, have a higher risk of breast cancer in relation to oral contraceptives and other risk factors for breast cancer as compared with breast cancer cases without these tumor markers, or women without breast cancer.

Another comment from the reviewers was on our plan for the statistical analyses, specifically on our use of women without breast cancer (as well as breast cancer cases without the tumor marker) as our comparison groups. One reviewer suggested we restrict our comparison to only the tumor negative cases. We have reviewed the literature on this subject, and have talked to numerous experts across the U.S., including Dr. Alice Whittemore at Stanford University (personal communication, 1995). The consensus has been that we should use both comparison groups.

BODY

Study Methods

Collection of Pathology Specimens. We have requested pathology materials for the 511 breast cancer patients who participated in a previously conducted population-based, case-control study among women under age 45 in a five-county area of central New Jersey. In total, all forty-three eligible New Jersey Hospitals have been contacted. Pathology materials have been successfully collected on over half the sample of breast cancer cases (which represents 70% of all participating hospitals).

Laboratory Assays. Laboratory methods include: (i) review of the available materials (to determine the extent of the tumor tissue available for the analyses to ensure block is not depleted); (ii) preparation of the slides for the planned and future tumor marker assays; and (iii) the performance of the laboratory assays by immunohistochemistry. Assays have been completed for over a third of cases with available tissue to date.

Statistical Analyses. Data entry of laboratory results has begun. Statistical analyses will begin when the laboratory assays are complete.

Study Progress

1. Hospitals

Number of New Jersey Hospitals eligible.....43 (100%)
Number of New Jersey Hospitals with requests completed.....30 (70%)
Number of New Jersey Hospitals with outstanding requests.....13 (30%)

2. Patients

Total number of patients.....511 (100%)
Patients with no requests made because hospitals are out of state 8 (1.6%)
Total number of patients with requests made 503 (98.4%)
Number of patients with all available materials received.....268 (52.5%)
Patients with neither blocks or slides available.....18 (3.5%)
Number of patients with some requests outstanding.....22 (4.3%)
Number of patients with no requests received yet.....195 (38.2%)

3. Laboratory Review and Analyses

Number of patients with blocks available for use by Dr. Hibshoosh's lab.....268 (100%)
Number of patients currently being reviewed by Dr. Hibshoosh.....109 (41%)
Number of patients not yet given to Dr. Hibshoosh.....67 (25 %)
Number of patients with completed review, cutting, and staining 92 (34%)

4. Minority Participation

Of the original 511 cases who participated in the case-control study in New Jersey, and are eligible for our tumor marker study, 433 are white, 76 are black and other minorities, and 2 were of unknown ethnicity. Of the 509 with known ethnicity, 222 (51.3%) whites and 45 (59.2%) blacks and others are currently enrolled in the tumor marker study.

CONCLUSIONS

- As suggested by the study reviewers, we have successfully obtained other funding to include other tumor markers besides HER-2/*neu*. Thus, we have expanded the study hypothesis to include exploration of an interaction between risk factors for breast cancer and p53 or cyclin D1.

- We have successfully retrieved over half of the tumor specimens required for the study.

- We have prepared the specimens and completed laboratory assays on over a third of all cases.

- Minority participation is comparable to the participation rate among non-minority women..

- Study progress to date is on target for successful completion of the study by the end of year two.